

**UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS**

ASTELLAS INSTITUTE FOR REGENERATIVE
MEDICINE, and STEM CELL & REGENERATIVE
MEDICINE INTERNATIONAL, INC.,

Plaintiffs,

v.

IMSTEM BIOTECHNOLOGY, INC., XIAOFANG
WANG, and REN-HE XU,

Defendants.

C.A. No. 1:17-cv-12239

**LEAVE TO FILE GRANTED
ON 8/21/19 (DKT. 85)**

DEFENDANTS' AMENDED ANSWER AND COUNTERCLAIMS

Defendants ImStem Biotechnology, Inc. (“ImStem”) Dr. Xiaofang Wang, M.D., Ph.D. (“Dr. Wang”) and Dr. Ren-He Xu (“Dr. Xu”) (collectively “Defendants”) hereby Answer the Complaint of plaintiffs Astellas Institute for Regenerative Medicine (“Astellas”) and Stem Cell & Regenerative Medicine International, Inc. (“SCRMI”) (collectively “plaintiffs”) as follows:

INTRODUCTION

1. Defendants admit that this action concerns the creation of mesenchymal stem cells and that the mesenchymal stem cells are useful in treating various disorders, including multiple sclerosis. Defendants deny the remaining allegations contained in Paragraph 1.

2. Defendants admit that Astellas and SCRMI focus on research regarding regenerative medicine. Defendants further admit that Dr. Lu and Dr. Lanza published an article in Nature Methods in 2007 on a method for generating hemangioblasts from embryonic stem cells. Defendants admit that hemangioblasts are a specialized type of progenitor cell derived from human embryonic stem cells that are useful in the field of regenerative medicine because

they can be differentiated into a number of different cell types used for the treatment of various diseases. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained Paragraph 2.

3. Defendants admit that Dr. Kimbrel and Dr. Lanza developed a method for differentiating embryonic stem cells into mesenchymal stem cells via a hemangioblast intermediate. Defendants deny that Dr. Kimbrel and Dr. Lanza thought of the idea of using the mesenchymal stem cells they created to treat autoimmune diseases like multiple sclerosis. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained Paragraph 3.

4. Defendants deny that SCRMI was a small company at the time. Upon information and belief, SCRMI was a subsidiary of a publicly traded company. Defendants admit the remaining allegations contained in Paragraph 4.

5. Defendants deny that Dr. Lu knew that defendants had access to the EAE mouse model. Defendants admit that Dr. Lu introduced Dr. Wang to Dr. Kimbrel to discuss a potential collaboration in response to an inquiry from Dr. Wang. Defendants admit that Dr. Kimbrel and Dr. Wang corresponded. Defendants admit that plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with defendants for purposes of the collaboration. Defendants admit that Dr. Xu submitted a grant application in January 2011 for further studies on the use of MSCs in the EAE model. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 5.

6. Defendants admit that the test results from the EAE mouse experiments were positive and that Dr. Kimbrel, Dr. Xu and Dr. Wang worked together on an article that was

published in Stem Cell Reports in July 2014. Defendants deny the remaining allegations contained in Paragraph 6.

7. Defendants admit that Dr. Xu and Dr. Wang formed ImStem in or about June 2012 and filed Application No. 14/413,290 with the United States Patent and Trademark Office, which became Patent No. 9,745,551 (the “551 Patent”). Defendants further admit that they represented to the PTO that they had invented a method for differentiating mesenchymal stem cells from hemangioblasts using a GSK3 inhibitor and feeder free culture medium. Defendants deny the remaining allegations contained in Paragraph 7.

8. Denied.

NATURE OF THE ACTION

9. Paragraph 9 contains legal conclusions to which no response is required.

THE PARTIES

10. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 10.

11. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 11.

12. Admitted.

13. Admitted.

14. Defendants admit that Dr. Xu was the Chief Scientific Officer of ImStem as well as one of ImStem’s founders and is currently employed by the University of Macau. Defendants deny the remaining allegations contained in Paragraph 14.

SUBJECT MATTER JURISDICTION AND VENUE

15. Paragraph 15 contains legal conclusions to which no response is required.

16. Paragraph 16 contains legal conclusions to which no response is required.

17. Paragraph 17 contains legal conclusions to which no response is required.

PERSONAL JURISDICTION

18. Admitted.

19. Admitted.

20. Defendants admit that Dr. Wang and Dr. Xu visited plaintiffs' facility in Marlborough, Massachusetts during their collaboration with Dr. Kimbrel and Dr. Lanza for various reasons, including to collect cells and other materials necessary for their work in the collaboration. Defendants deny the remaining allegations contained in Paragraph 20.

21. Admitted.

22. Admitted.

23. Admitted. Further answering Paragraph 23, Defendants aver that they had their own grant funding to conduct the MSC studies and often used their own grant funds to purchase materials in furtherance of the collaboration.

24. Defendants admit that they traveled to plaintiffs' Marlborough, Massachusetts facility during their collaboration. Defendants deny the remaining allegations contained in Paragraph 24.

25. Paragraph 25 contains legal conclusions to which no response is required.

26. Paragraph 26 contains legal conclusions to which no response is required.

27. Paragraph 27 contains legal conclusions to which no response is required.

28. Paragraph 28 contains legal conclusions to which no response is required.

FACTUAL BACKGROUND

Plaintiffs' Development of Methods for Generating Mesenchymal Stem Cells

29. Defendants admit that Dr. Kimbrel and Dr. Lanza developed a method for generating hemangioblasts. Defendants admit that hemangioblasts are a specialized type of progenitor cell derived from human embryonic stem cells that are useful in the field of regenerative medicine because they can be differentiated into a number of different cell types used for the treatment of various diseases. Defendants deny the remaining allegations contained in Paragraph 29.

30. Defendants admit that Dr. Lu and Dr. Lanza, along with others, published an article in Nature Methods in 2007 on a method for generating hemangioblasts from embryonic stem cells. Defendants aver that the article published by the journal Nature Methods speaks for itself and requires no further response.

31. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 31.

32. Defendants deny that Dr. Kimbrel and Dr. Lanza thought of the idea to use the mesenchymal stem cells they created to treat autoimmune diseases like multiple sclerosis. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained Paragraph 32.

Plaintiffs' Collaboration with Drs. Xu and Wang

33. Defendants deny that Dr. Kimbrel and Dr. Lanza sought to find collaborators with animal facilities and experience with animal models of autoimmune diseases, including the EAE mouse model. Defendants admit the remaining allegations contained in Paragraph 33.

34. Defendants admit Dr. Lu introduced Dr. Kimbrel to Dr. Wang about a potential

collaboration and that Dr. Wang suggested testing the mesenchymal stem cells in the EAE mouse model. Defendants deny that Dr. Lu knew that they had access to the EAE mouse model. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 34.

35. Defendants admit that they visited SCRMI in or about August 2010 and collected frozen MSCs for experiments in furtherance of the parties' collaboration. Defendants further admit that, following the meeting at SCRMI, Dr. Kimbrel shared a protocol for differentiating hemangioblasts into MSCs based largely on the protocol that Dr. Lu and Dr. Lanza had previously published in Nature Methods. Defendants deny the remaining allegations contained in Paragraph 35.

36. Defendants deny that Dr. Kimbrel and Dr. Lanza provided data that demonstrated that the cells generated from their protocol were, in fact, mesenchymal stem cells. Defendants admit the remaining allegations contained in Paragraph 36.

37. Admitted.

38. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 38.

39. Defendants admit that a Material Transfer Agreement was proposed but never executed. Defendants deny the remaining allegations contained in Paragraph 39.

40. Defendants admit that in the course of the parties' collaboration, and in connection with the work performed by defendants during that collaboration, they requested certain supplies from Drs. Kimbrel and Lanza.

41. Admitted.

42. Denied.

43. Defendants admit that they continued collaborating with Dr. Kimbrel and Dr. Lanza during 2012 through 2013, including working together to draft an article that was published in Stem Cell Reports. Defendants further admit that discord developed as a result of Dr. Kimbrel and Dr. Lanza's decision to publish their own paper separately in a lesser-known journal, causing the collaboration's paper to be rejected from the journal to which it was submitted for publication Cell Stem Cell. Defendants deny all remaining allegations contained in Paragraph 43.

44. Admitted.

45. Admitted.

Dr. Xu and Dr. Wang Form ImStem and File Patent Application

46. Defendants admit that in or about June 2012, they formed ImStem Biotechnology, Inc. and were awarded funding and lab space for stem cell research. Defendants deny the remaining allegations contained in Paragraph 46.

47. Defendants admit that in or about July 2012 and February 2013, they filed the provisional applications that led to the '551 Patent. The '551 Patent claims a method for differentiating hESCs into MSCs using a GSK3 inhibitor and feeder free culture medium. Dr. Wang's method is materially different from the protocol that Dr. Kimbrel shared with Dr. Wang for purposes of their collaboration. Dr. Wang developed his method through his own efforts, separate and apart from the work of the collaboration. Dr. Wang further never disclosed the GSK3 inhibitor method to Dr. Kimbrel or anyone else. Defendants deny the remaining allegations contained in Paragraph 47.

48. Defendants admit that they knew Dr. Kimbrel and Dr. Lanza had filed a patent application on their protocol for differentiating hemangioblasts into MSCs. Defendants further

admit that they signed a declaration dated January 12, 2017, stating that they possessed the subject matter of the '551 Patent before November 30, 2011. Further answering Paragraph 48, defendants state that they believed Dr. Kimbrel and Dr. Lanza's protocol for differentiating MSCs contained only obvious, public information. Defendants therefore did not believe that Dr. Kimbrel and Dr. Lanza had contributed anything significant to Dr. Wang's method of differentiating MSCs using a GSK3 inhibitor and feeder free culture medium.

49. Admitted.

50. Defendants admit that plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with defendants for purposes of the collaboration. Defendants deny that the '551 Patent claims plaintiffs' technology. Dr. Wang developed the method claimed in the '551 through his own efforts, separate and apart from the work of the collaboration. Defendants deny the remaining allegations contained in Paragraph 50.

COUNT I

(Correction of Inventorship for the '551 Patent: Drs. Kimbrel and Lanza as Sole Joint Inventors)

51. Defendants' answers to Paragraphs 1-50 are incorporated herein by reference.

52. Denied.

53. Denied.

54. Denied.

COUNT II

(In the Alternative, Correction of Inventorship for the '551 Patent: Drs. Kimbrel and Lanza as Joint Inventors with the Currently Named Inventors)

55. Defendants' answers to Paragraphs 1-54 are incorporated herein by reference.

56. Denied.

57. Defendants lack knowledge or information sufficient to admit or deny the

allegations in Paragraph 57.

58. Denied.

COUNT III
(Conversion)

59. Defendants' answers to Paragraphs 1-58 are incorporated herein by reference.

60. Defendants admit that plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with defendants for purposes of the collaboration. Defendants deny that plaintiffs initially shared this information under strict restrictions regarding its use. Defendants deny the remaining allegations contained in Paragraph 60.

61. Denied.

62. Denied.

63. Denied.

COUNT IV
(Unjust Enrichment)

64. Defendants' answers to Paragraphs 1-63 are incorporated herein by reference.

65. Denied.

66. Denied.

67. Denied.

68. Denied.

69. Denied.

70. Denied.

COUNT V
(Unfair Trade Practices Under Massachusetts General Law Chapter 93A)

71. Defendants' answers to Paragraphs 1-70 are incorporated herein by reference.

72. Paragraph 72 contains legal conclusions to which no response is required.

73. Denied.

74. Denied.

75. Denied.

76. Denied.

COUNT VI
(Misappropriation of Trade Secrets)

77. Defendants' answers to Paragraphs 1-76 are incorporated herein by reference.

78. Defendants admit that they received certain scientific information relating to the generation of MSCs during the course of the parties' collaboration. Defendants deny the remaining allegations contained in Paragraph 78.

79. Defendants admit that sometime after the parties' collaboration had commenced Dr. Kimbrel sought assurances that any new information shared by plaintiffs going forward would be treated confidentially for the purposes of further collaboration between the parties. Defendants deny the remaining allegations contained in Paragraph 79.

80. Denied.

81. Denied.

COUNT VII
(Negligent Misrepresentation)

82. Defendants' answers to Paragraphs 1-81 are incorporated herein by reference.

83. Defendants admit that sometime after the parties' collaboration had commenced Dr. Kimbrel sought assurances that any new information shared by plaintiffs going forward would be treated confidentially for the purposes of further collaboration between the parties. Defendants further admit that on or about January 12, 2017 they filed a declaration with the

United States Patent and Trademark Office declaring that they are the original inventors of the subject matter of the '551 Patent. Defendants deny the remaining allegations contained in Paragraph 83.

84. Denied.

JURY DEMAND

85. Paragraph 85 does not require a response.

PRAYER FOR RELIEF

86. Defendants deny that plaintiffs are entitled to the relief requested in the Complaint. To the extent that any statement in the Prayer for Relief is deemed factual, it is denied.

AFFIRMATIVE DEFENSES

Further answering the Complaint, defendants assert the following defenses, without assuming the burden of proof where such burden would otherwise be on the plaintiff. Defendants reserve the right to assert additional defenses as further information is obtained.

**FIRST AFFIRMATIVE DEFENSE
(Failure to State a Claim)**

The Complaint fails to state a claim upon which relief may be granted.

**SECOND AFFIRMATIVE DEFENSE
(Laches)**

Plaintiffs' claims are barred, in whole or in part, by the doctrine of laches.

**THIRD AFFIRMATIVE DEFENSE
(Unclean Hands)**

Plaintiffs' claims are barred, in whole or in part, by the doctrine of unclean hands.

**FOURTH AFFIRMATIVE DEFENSE
(Statute of Limitations)**

Plaintiffs' claims are barred, in whole or in part, by the applicable statute of limitations.

AMENDED COUNTERCLAIMS

Defendants bring the following Amended Counterclaims against plaintiffs for Correction of Inventorship of U.S. Patent No. 8,961,956 (“the ‘956 Patent”) (Exhibit A), U.S. Patent No. 8,962,321 (the “‘321 Patent”) (Exhibit A-1), and unjust enrichment.

NATURE OF THE ACTION

1. This case involves a scientific collaboration in the field of stem cell research. The parties collaborated for a period of years on research involving a specialized type of stem cell called a mesenchymal stem cell (“MSC”).

2. At the outset of the collaboration, Dr. Wang and Dr. Xu suggested that the parties study MSC’s functionality in treating autoimmune disorders, including multiple sclerosis. Dr. Wang conducted all of the *in vivo* animal studies for the MSC collaboration and shared his resulting data with plaintiffs.

3. Unbeknownst to Dr. Wang and Dr. Xu, plaintiffs filed a provisional patent application with the United States Patent and Trademark Office (“PTO”) claiming as their own the use of MSCs in autoimmune treatment. The provisional application also incorporated Drs. Wang and Xu’s *in vivo* data. Furthermore, the plaintiffs copied verbatim language drafted by Dr. Wang into the specification and incorporated his and Dr. Xu’s inventive contributions concerning certain features of the cells themselves, as well as additional inventive contributions. In short, plaintiffs took advantage of Dr. Wang’s experience with autoimmune disorders and his and Dr. Xu’s ideas and data concerning the efficacy of MSCs on the EAE model and claimed it as their own.

PARTIES

4. ImStem Biotechnology Inc. is a Connecticut biotechnology company with a principal place of business at 400 Farmington Ave., R1808, Farmington, Connecticut 06030.

5. Dr. Xiaofang Wang is the Chief Technology Officer and Vice President and a founder of Imstem with a place of business at 400 Farmington Ave., R1808, Farmington, Connecticut 06030.

6. Upon information and belief, Astellas Institute for Regenerative Medicine is a Delaware corporation with a principal place of business at 33 Locke Drive, Marlborough, Massachusetts 01752.

7. Upon information and belief, Stem Cell & Regenerative Medicine International, Inc. is a Delaware corporation which had its principal place of business at 33 Locke Drive, Marlborough, Massachusetts 01752.

JURISDICTION AND VENUE

8. This Court has subject matter jurisdiction over Defendants' counterclaims pursuant to 28 U.S.C. §§ 1331, 1338, and 1367.

9. Venue is proper under 28 U.S.C. § 1391(b)(1) because plaintiffs reside within the District.

10. The Court has personal jurisdiction over plaintiffs because they are residents of Massachusetts.

BACKGROUND

Science Background

11. Human embryonic stem cells ("hESCs") are pluripotent, meaning they have the remarkable ability to develop into any type of specialized cell found in the human body. In the prior art, hESCs were derived from frozen human fertilized eggs. Ethical considerations led scientists to develop methods of growing stem cells in culture in a laboratory, paving the way to greater study and research of stem cells in the treatment of various diseases.

12. This case involves a protocol to induce hESCs into a more specialized type of stem cell (MSCs), through a process known as differentiation. MSCs have multiple potentialities in that they can differentiate into bone, cartilage, adipose and other connective tissues.

13. The focus of most research and development of stem cells has been in the field of regenerative medicine. Regenerative medicine is the process of creating living, functional tissues to repair or replace tissue or organ function that has been lost due to age, disease, damage, or congenital defects. Many researchers in the area of regenerative medicine are working to understand how stem cells, and MSCs in particular, can be used to grow healthy tissue in a lab or to repair damaged tissues inside the body to treat a variety of degenerative conditions such as heart failure, tissue damage, arthritis and bone fractures.

14. Stem cells also hold great potential in other fields of medicine. For example, in the field of autoimmune disorders, researchers are studying how stem cells could be used to treat the inflammation process at the heart of a number of autoimmune disorders. Multiple sclerosis is a chronic autoimmune disorder that affects 2.5 million people worldwide. The hallmark of the disorder is a build-up of inflammatory plaques. Efforts to reduce inflammation in multiple sclerosis patients using systemic anti-inflammatory agents have been limited due to severe side effects. Scientists working in the field of autoimmune disorders have discovered that MSCs inhibit the activation of lymphocytes, and the release of pro-inflammatory cytokines (small proteins involved in immunomodulation) and promote the regeneration of damaged cells. MSCs could be a break-through therapy for multiple sclerosis patients.

Factual Background

15. Dr. Wang has extensive experience in the field of autoimmune disease. While working at Yale University School of Medicine, Dr. Wang studied the precise genetic

mechanism for autoimmune disease in the experimental autoimmune encephalopathy (“EAE”) mouse model. The EAE mouse develops paralysis over time and is the closest proximity mouse model for multiple sclerosis. At the core of the inflammatory process that causes multiple sclerosis are white blood cells called lymphocytes. Dr. Wang and his team discovered that a particular type of lymphocyte (Th17) causes mice to be genetically predisposed to developing multiple sclerosis. In May 2010, Dr. Wang and his colleagues submitted a paper to Cell Press Immunity reporting their discovery. (Exhibit B.)

16. In or about 2009, Dr. Wang received a grant to study a new method of differentiating hESCs into another type of specialized stem cell. Dr. Wang’s mentor, Dr. Ren-He Xu was friendly with a colleague, Dr. Shi-Jiang Lu, who worked at SCRMI.

17. In July 2010, Dr. Xu set up a meeting with Dr. Lu to discuss Dr. Wang’s work and a potential collaboration on his grant-funded research. At that meeting, Drs. Xu and Wang proposed that they also collaborate to test the effectiveness of hemangioblast-derived MSCs (“HB-MSCs”) to treat autoimmune disease – Dr. Wang’s area of expertise. Drs. Wang and Xu specifically proposed multiple sclerosis. Dr. Lu suggested that Dr. Wang get in touch with his colleagues, Drs. Kimbrel and Lanza, to discuss collaborating on HB-MSCs.

18. In their initial email exchange, Dr. Wang suggested to Dr. Kimbrel that their collaboration focus on testing the effectiveness of HB-MSCs to treat autoimmune disease – his area of expertise. In particular, in light of his recent research and experience at Yale, he suggested that they use the EAE mouse model to test the HB-MSC’s functionality to treat multiple sclerosis.

19. As noted in the Complaint, Astellas and SCRMI “have been at the forefront of research regarding regenerative medicine and cell therapy.” (Compl. ¶ 2.) Coming from the

field of regenerative medicine, Dr. Kimbrel and Dr. Lanza's research was focused on the functionality of stem cells in treating degenerative conditions. At the time that they met Drs. Wang and Xu, Drs. Kimbrel and Lanza were not familiar with MSC's anti-inflammatory abilities or their potential application in the area of autoimmune disease.

20. Nor did Dr. Kimbrel or Dr. Lanza have any direct familiarity or experience with the EAE mouse model. In an email to Dr. Wang, Dr. Kimbrel stated "I am not familiar with the EAE mouse model and am curious as to your thoughts on how you would use these cells in a model for autoimmune disease. If you have any relevant papers you could send my way, that would be great."

21. In response, Dr. Wang sent links to several journal articles and explained that several labs had "found some mechanism of how MSC suppresses immune function" but noted "[c]urrently, no lab has tested the hESC-MSK to treat mouse EAE model yet."

22. After reviewing the articles, Dr. Kimbrel agreed it would be interesting to see whether the HB-MSKs had any autoimmune suppression effect. She suggested that they have an in person meeting to discuss a collaboration.

23. A meeting took place at SCRMI in early August 2010, after which Dr. Wang and Dr. Kimbrel immediately began collaborating on the HB-MSK project.

24. During the collaboration, Dr. Wang conducted *in vivo* experiments on the EAE model. At various times, Dr. Wang sent the resulting data to Dr. Kimbrel. The results were promising. The team later worked together to write up the results, which were ultimately published in two journals.

25. During the collaboration, Dr. Wang did not have access to the MA-09 hESC cell line developed by Dr. Kimbrel. Plaintiffs did not have access to other hESC cell lines (e.g. CT2,

H9, and Envy hESC) with which to confirm that the MSCs they had differentiated from hemangioblasts were, in fact, MSCs. Defendants performed this work by confirming that hemangioblasts could be differentiated into MSCs from multiple hESC cell lines. Subsequently, a controversy arose over whether MA-09 is a true hESC cell line.

26. During the course of the collaboration, Drs. Wang and Xu began making their own modifications to the HB-MSC protocol – including changing the first step, adding glycogen synthase kinase-3 inhibitor to make HB-MSCs under feeder-free, serum-free, defined-culture conditions, mitotically inactivating the resulting cells, and chemically “characterizing” the cells (*e.g.* as to the anti-inflammatory cytokine IL-6) and comparing them to bone-marrow-derived MSCs. Drs. Wang and Xu told Dr. Kimbrel about these inventive modifications.

27. During the course of the collaboration, at least as early as November 2010, Drs. Wang and Xu also conceived of the idea of mitotically inactivating the HB-MSCs (*e.g.* by irradiation) so that the cells, when used clinically, would be unable to divide/reproduce/differentiate into unwanted cell types (*e.g.* cancer tumors), while still retaining their therapeutic effect. Again, Drs. Wang and Xu told Dr. Kimbrel about these inventive modifications.

28. On November 30, 2011, Dr. Kimbrel and Dr. Lanza filed provisional patent application No. 61/565,358 with the PTO. Plaintiffs’ provisional application (and later applications) included data from the *in vivo* experiments Dr. Wang conducted on the EAE mouse model during the parties’ MSC collaboration. (Exhibit C.)

29. The PTO subsequently issued two patents stemming from plaintiffs’ provisional application: the ‘956 Patent and Patent No. 8,962,321 (the “‘321 Patent”).

30. Claim 1 of the ‘956 Patent claims a method for culturing hemangioblasts under

conditions that give rise to MSCs. Claims 3 and 4 of the '956 Patent claim the use of the method of claim 1 in the treatment of autoimmune disorders, including multiple sclerosis.

31. The '956 Patent names Dr. Kimbrel and Dr. Lanza, along with two of their colleagues, as the sole inventors.

32. The '321 Patent names Dr. Kimbrel and Dr. Lanza, along with two of their colleagues, as the sole inventors.

33. Claims 17 and 18 of the '321 Patent claim HB-MSCs that have been mitotically inactivated in preparation for clinical use, Drs. Wang and Xu's idea. Claim 21 claims HB-MSCs having a potency greater than bone-marrow-derived MSCs, Drs. Wang and Xu's idea. The '321 Patent specification included text copied verbatim from Dr. Wang's 2010 grant application.

COUNT I
(CORRECTION OF INVENTORSHIP FOR THE '956 PATENT, 35 U.S.C. § 256)

34. Defendants Dr. Wang and ImStem repeat and reallege the allegations in paragraphs 1 through 33 of the Amended Counterclaims as if fully set forth herein.

35. Before meeting Dr. Wang, Dr. Kimbrel and Dr. Lanza were planning to research MSC's functionality in treating degenerative disease. They were unaware of MSC's potential use in the field of autoimmune disorders.

36. The use of MSCs in the treatment of autoimmune disorders is a highly valuable aspect of the invention that gave rise to the '956 Patent. Dr. Wang contributed this idea.

37. Dr. Kimbrel and Dr. Lanza (along with their colleagues) filed a provisional patent application claiming Drs. Wang's ideas of using MSCs in the treatment of autoimmune disorders as their own. On February 24, 2015, the '956 Patent issued.

38. Through omission, inadvertence, and/or error Dr. Wang was not listed as a co-inventor on the '956 Patent.

39. The omission, inadvertence, and/or error occurred without any deceptive intent on the part of Dr. Wang.

40. Upon information and belief, Astellas intends to commercialize the method claimed in the '956 Patent for the treatment of autoimmune disorders.

41. Dr. Wang is a joint inventor of the subject matter of the '956 Patent and should be added to the individuals currently named as inventors.

COUNT II
(CORRECTION OF INVENTORSHIP FOR THE '321 PATENT, 35 U.S.C. § 256)

42. Defendants repeat and reallege the allegations in paragraphs 1 through 41 of the Amended Counterclaims as if fully set forth herein.

43. The idea of mitotically inactivating HB-MSCs in preparation for clinical use is a highly valuable aspect of the invention that gave rise to the '321 Patent. Drs. Wang and Xu contributed this idea. The idea of HB-MSCs comparing HB-MSCs to bone-marrow-derived MSCs and determining greater potency is a valuable aspect of the invention that gave rise to the '321 Patent. Drs. Wang and Xu contributed this idea.

44. Dr. Kimbrel and Dr. Lanza (along with their colleagues) filed a provisional patent application claiming Drs. Wang and Xu's ideas as their own. On February 24, 2015, the '321 Patent issued.

45. Through omission, inadvertence, and/or error Dr. Wang and Xu were not listed as a co-inventors on the '321 Patent.

46. The omission, inadvertence, and/or error occurred without any deceptive intent on the part of Drs. Wang and Xu.

47. Upon information and belief, Astellas intends to commercialize the methods claimed in the '321 Patent.

48. Drs. Wang and Xu are joint inventors of the subject matter of the ‘321 Patent and should be added to the individuals currently named as inventors.

COUNT III
(UNJUST ENRICHMENT)

49. Defendants repeat and reallege the allegations in paragraphs 1 through 48 of the Amended Counterclaims as if fully set forth herein.

50. During the course of the parties’ collaboration, Dr. Wang conducted all of the *in vivo* experiments on the EAE mouse model (which was then used in the patent applications leading to the ‘956 and ‘321 Patents).

51. By their own admission, SCRMI was a small company at the time and plaintiffs did not have the ability to conduct their own animal testing. (Compl. ¶ 9.)

52. At various times during the collaboration, Dr. Wang reported the data from his EAE experiments to Dr. Kimbrel. For example, on December 9, 2010, Dr. Kimbrel requested that Dr. Wang send her a graph reporting on the EAE results for a presentation she intended to share with SCRMI’s Chief Scientific Officer. Dr. Wang provided Dr. Kimbrel with a chart containing his data. Defendants’ *in vivo* data was also incorporated into a grant application that was submitted in January 2011 and shared with plaintiffs.

53. At various times during the collaboration, Drs. Wang and Xu shared with Dr. Kimbrel the various inventive ideas and additions they made to the HB-MSD protocol.

54. Upon information and belief, plaintiffs included that same *in vivo* data chart in support of an Example in provisional patent application No. 61/565,358, which they filed with the PTO.

55. Upon information and belief, plaintiffs included the same Example in nonprovisional applications claiming priority to the provisional application.

56. Upon information and belief, plaintiffs deleted the chart in the nonprovisional applications and replaced reference to it with “Data not shown”.

57. Deletion of the chart in the nonprovisional applications is evidence of plaintiffs’ knowledge of their wrongful conduct in using Dr. Wang’s data in their patent applications.

58. In reliance on plaintiffs’ provisional application and nonprovisional applications, as well as other inventive concepts contributed by the Defendants, the PTO issued two patents to plaintiffs: the ‘956 Patent and the ‘321 Patent.

59. Defendants conferred a benefit on plaintiffs by conducting the *in vivo* EAE animal studies and disclosing their data to plaintiffs in furtherance of the collaboration.

60. Plaintiffs retained the benefit conferred by defendants by including the data and inventive concepts from Dr. Wang’s *in vivo* EAE studies in their provisional patent application.

61. Plaintiffs have been unjustly enriched by the issuance of two valuable patents, both of which relied, in part, on the data that was generated exclusively by defendants.

62. It would be inequitable for plaintiffs to retain the benefit of the ‘956 and ‘321 Patents under these circumstances.

63. Defendants lack an adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE Defendants respectfully request this Court enter judgment in their favor as follows:

A. Pursuant to 35 U.S.C. §256, an order that the Director of the United States Patent and Trademark Office correct the inventorship of United States Patent No.

8,961,956 to name Xiaofang Wang as co-inventor;

B. Pursuant to 35 U.S.C. §256, an order that the Director of the United States

Patent and Trademark Office correct the inventorship of United States Patent No. 8,962,321 to name Xiaofang Wang and Ren-He Xu as co-inventors;

C. A declaration that Xiaofang Wang is a co-inventor of the ‘956 Patent;

D. A declaration that Xiaofang Wang and Ren-He Xu are co-inventors of the ‘321 Patent;

E. An order for a constructive trust over all of plaintiffs’ intellectual property – including, but not limited to, provisional patent application No. 61/565,358, application No. 14/629,383, the ‘956 Patent, and the ‘321 Patent – which reflects, incorporates, or relied upon data and inventive concepts from the *in vivo* research Drs. Wang and Xu conducted during the parties’ collaboration;

F. An award of reasonable costs and attorney’s fees pursuant to 35 U.S.C. § 256; and

G. All such further and additional relief as the Court deems just and proper.

August 28, 2019

Respectfully submitted,

DEFENDANTS IMSTEM
BIOTECHNOLOGY, INC., DR.
XIAOFANG WANG, and DR. REN-HE XU

By their attorneys,

/s/ Timothy R. Shannon
Timothy R. Shannon, MA Bar # 655325
VERRILL DANA LLP
One Portland Square
P.O. Box 586
Portland, Maine 04112-0586
(207) 774-4000
tshannon@verrilldana.com

Benjamin M. Stern, MA Bar # 646778
VERRILL DANA LLP
One Federal Street
Boston, Massachusetts 02108
(617) 309-2600
bstern@verrilldana.com

CERTIFICATE OF SERVICE

I hereby certify that on August 28, 2019, I caused a true copy of the foregoing document to be served upon all counsel of record via the Court's CM/ECF electronic filing system.

/s/ Timothy R. Shannon
Timothy R. Shannon